Abstract

Grant Number: 1 X01 MH077628-01
PI Name: HARSAY, EDINA
PI Email: HARSAY@KU.EDU
PI Title: ASSISTANT PROFESSOR
Project Title: Chemical Genetics Screens to Identify Modulators of Post-Golgi Transport

Abstract: *DESCRIPTION* (provided by applicant): Membrane vesicle and tubule-mediated intracellular transport of proteins and lipids is an essential process in all eukaryotic cells. The regulation of membrane transport pathways is required for the control of cell growth and division as well as for maintaining normal cell function and homeostasis of non-dividing cells. The long-term goal of the Harsay laboratory is to define the molecular mechanisms by which cargo is transported from the Golgi to the cell surface, so that improved therapeutic strategies to treat diseases involving transport dysfunction can be developed. Many of the components of the transport machinery have been described for several transport steps and shown to be highly conserved among eukaryotes. However, the complexity and branching of the late, post-Golgi, exocytic pathway has made it difficult to identify proteins that function at late transport steps, and the molecular machinery required for exocytic cargo sorting and exit from the Golgi is still largely unknown. The objective of this application is to identify components of the post-Golgi transport machinery by using a chemical genetic approach. The strategy involves a mutant yeast strain having a block in one branch of the post-Golgi exocytic pathway. By using this strain in high-throughput, cell-based phenotypic screens of diverse compound libraries, it is expected that compounds that target specifically regulators or structural components of the post-Golgi transport machinery will be discovered. Identifying compound targets and target interactors, as well as using biologically active small molecules as tools in the molecular dissection of membrane and protein traffic steps, will result in a better understanding of late secretory transport mechanisms and of the diseases that involve perturbations of these mechanisms. Such diseases include diabetes, neurological and immune disorders, and cancer. Furthermore, many intracellular pathogens exploit host cell transport mechanisms for their survival and proliferation. Therefore, the knowledge and tools gained from this work will allow better understanding of the etiology and pathophysiology of many human diseases, as well as ultimately suggest strategies for therapeutic interventions to prevent and treat such diseases.

Thesaurus Terms:
High throughput screening, Post-Golgi Transport, exocytic pathway, cell-based phenotypic screen, secretory transport, diabetes, neurological disorders, immune disorders, cancer, Chemical Genetics, eukaryotic cell

Institution: UNIVERSITY OF KANSAS
2385 IRVING HILL ROAD
CTR FOR RESEARCH INC.
LAWRENCE, KS 66045-7563
Fiscal Year: 2006
Department: DEPARTMENT OF MOLECULAR BIOSCIENCES

Project Start: 2006/02/01
Project End: 2007/01/31
ICD: NATIONAL INSTITUTE OF MENTAL HEALTH
IRG: ZMH1